

chronic organic mitral endocarditis. This is 8 per cent. of all the autopsies analyzed and 13.6 per cent. of those under the age of fifty. In striking contrast is the fact that only 1.9 per cent. of the patients dying at an older age showed organic mitral endocarditis pathologically.

CONCLUSIONS. From a study of 128 consecutive cases of auricular fibrillation diagnosed by electrocardiograms, and of 261 consecutive autopsies the following general conclusions may be drawn.

1. Auricular fibrillation is a very common condition in a general hospital being met with almost as frequently as lobar pneumonia.

2. Syphilis plays an unimportant role in the etiology of auricular fibrillation.

3. The transient form of auricular fibrillation is much more common than is ordinarily believed. Careful observations and electrocardiographic tracings are necessary in order to avoid missing the transient cases.

4. About one-third of the cases of persistent auricular fibrillation have had one or more attacks of rheumatic fever or chorea and show clinical signs of chronic organic mitral endocarditis. The average age of these patients is about thirty-seven years. About one-third of the cases have not had rheumatic fever or chorea and show no signs of chronic organic mitral endocarditis. The average age of these patients is about fifty-eight years. About one-third of the cases fall into neither Group I or II.

5. Chronic organic mitral endocarditis is quite infrequently found in patients over fifty years of age either in the living as a result of physical examination or in the dead by postmortem examination.

6. Most patients with organic mitral disease develop mitral stenosis and only a small number reach the age of fifty years.

7. The application of these principles in the properly selected cases will aid in the diagnosis of cardiac conditions, giving particular help in the differentiation of relative and organic mitral insufficiency.

TYPHOID MENINGITIS: WITH REPORT OF A CASE.

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THE cerebrospinal and meningeal manifestations of human infection with typhoid bacillus have an abruptness of onset, a distinctiveness of symptoms, and a prognostic value which demand

unusual attention. They may also possess an importance independent of an association with the disease typhoid fever, sufficient to render unsuitable the customary designation of "complications" or "meningeal accidents." Several cases (Nos. 6, 12, 14, 16, Table II) have been reported under the caption of "primary typhoid meningitis." In all of these, except No. 14, careful necropsies serve as the basis for the statement that the meningitis was the only evidence of typhoid infection. Lavensen believes that in the instance reported by him the nasal passage was the portal of entry. While these studies are not sufficiently conclusive to set aside the older conception that the gastro-intestinal tract is the only way by which the typhoid bacillus gains entrance to the human body, nevertheless they remove the categorical element from this dictum by indicating other possible routes of infection.

Since the study of all reported cases of meningeal disease in typhoid fever, published by Cole in 1904, it has been generally accepted that the meningeal symptoms of typhoid infection may be classified in three distinct groups. These are called:

I. *Meningism*. When there are symptoms of meningitis with no demonstrable meningeal lesions and no abnormality of the spinal fluid.

II. *Serous Meningitis*. When the symptoms of meningitis are associated with non-suppurative lesions of the meninges and a spinal fluid, showing increased tension and containing *B. typhosus*.

III. *Purulent Meningitis*. When the meningitis is suppurative. Here the purulent spinal fluid contains typhoid bacilli.

MENINGISM. The occurrence of meningism, or symptoms of mild, transient meningeal irritation in cases of typhoid fever, is probably so common that this syndrome no longer moves the observer to record it in the medical journals. Annual reports of this condition in the literature of typhoid fever since 1904 do not equal in number the examples of so-called "meningism" seen in this hospital during the usual summer's experience with typhoid patients.

The absence of published records of this feature of typhoid fever does not, however, signify that the symptoms are not to be regarded seriously, as possibly representing an early stage of a more dangerous process. Netter has found the mortality three times as great in cases of typhoid fever showing Kernig's sign as in those which do not exhibit it. It is obvious, therefore, that on the appearance of the signs of meningitis, efforts should be made to determine the degree of the disease of the central nervous system, and means should be directed toward the relief of these symptoms. Lumbar puncture, thus indicated, is the only means of obtaining certain information as to the meningeal condition, and at the same time, as

shown by some cases, greatly improves the condition of the patient by removing spinal fluid.

SEROUS MENINGITIS. Since 1904, instances of serous meningitis have been reported by a number of authors as follows:

TABLE I.—SUMMARY OF CASE REPORTS OF SEROUS MENINGITIS IN TYPHOID FEVER.

Case.	Year.	Author.	Spinal fluid.		
			Culture.	Pressure.	Cytology.
1	1904	Achard and Paiseau	Negative	Increased	Lymphocytosis.
2	1905	Schutze	Positive	Increased	
3	1905	Schutze	Positive	Increased	
4	1908	Silberberg	Positive	Increased	
5	1908	Nieter	Positive	Increased	
6	1909	Claret and Lyon-Caen	Positive	Increased	Polys., 60 per cent. Monos. 25 per cent.
7	1910	Stein	None	Increased	Great relief after lumbar puncture in all cases.
8	1910	Stein	Negative	Increased	
9	1910	Stein	Negative	Increased	
10	1910	Schwartz	Positive	Increased	Pleocytosis with mono-nuclears.
11	1910	Saquépée	Positive	Increased	Monos. 95 per cent.
12	1911	Stubner	Positive	Increased	Typhoid bacilli seen in smears. Globulin negative.
13	1912	Lesieur and Mareland	Positive	Increased	Noleukoeytic reaction.
14	1914	Hannes	Positive	Averaged 130 mm. water.	Cells were usually 11 per cu. mm. Globulin tests were negative.
15	1914	Hannes	Positive		
16	1914	Hannes	Positive		
17	1914	Hannes	Positive		

The few instances of typhoid serous meningitis seen in this clinic in the past ten years correspond to the typical cases summarized in Table I. It is seen from these observations that the spinal fluid in serous meningitis is slightly turbid, due to the mono-nuclear pleocytosis, and that it contains typhoid bacilli in considerable numbers. The cerebrospinal fluid in this state contains also agglutinins for *Bacillus typhosus*, active in dilutions as high as 1 to 100. Silberberg is of the opinion that antibacterial substances may explain the failure of organism to grow in cultures from fluids in which the bacilli are microscopically demonstrable. Serous meningitis may subside, especially after the withdrawal of the excess of spinal fluid by lumbar puncture, or it may be the early phase of a purulent meningitis. It clearly demonstrates the localization of the typhoid bacillus in the meninges. The pyrogenic potentiality of the Eberth bacillus in this location is of unfavorable prognostic significance. Claret and Lyon-Caen have shown that of 13 cases of serous meningitis with typhoid bacillosis of the spinal fluid, 8 recovered while 5 died, giving a mortality of 40 per cent. of cases of typhoid fever complicated by this condition.

TABLE II.—SUMMARY OF CASES OF PURULENT TYPHOID MENINGITIS.

Case.	Year.	Author.	Sex.	Age.	History.	Autopsy.	Bacteriology.	Remarks.
1	1902	Crouchet and Buard	M	13	On 35th day of typhoid sudden onset of meningitis; purulent fluid on lumbar puncture; death 2 days later	None	B. typhosus from spinal fluid; all cultural and serological reactions typical	Not cited by Cole.
2	1905	Raymond and Sircard	M	48	During convalescence from typhoid, onset of pains in back and legs; localized purulent meningitis of lumbar cord; cured by operation		Pure culture of B. typhosus from pus around spinal cord	Probably primary infection in lumbar vertebrae.
3	1905	McCrae, J.	M	..	Death on 14th day of disease, after stupor, rigidity and convulsions	Acute encephalitis	Blood culture positive for B. typhosus	Data deficient.
4	1905	Stäubli, C.	M	23	Four weeks after beginning of typhoid, sudden onset of meningitis; purulent spinal fluid; death 20 days after meningitis symptoms began	Typical lesions of typhoid fever, with purulent cerebrospinal meningitis	B. typhosus from purulent spinal fluid	
5	1905	Delille, A.	F	9	Signs of meningitis on 21st day of typhoid fever; turbid spinal fluid with lymphocytosis at first; death 7 days later	Usual lesions of typhoid fever; thin yellow purulent exudate on meninges	B. typhosus from spinal fluid before death and at autopsy	Definite stage of serous meningitis at onset.
6	1908	Lavenson	F	26	Onset of meningitis on 10th day of typical typhoid fever	Purulent cerebrospinal meningitis; no other lesions	B. typhosus, with all typical reactions from spinal fluid before and after death	No intestinal lesions; no blood culture made; white blood cells, 20,040.
7	1908	Gurd and Nelles	M	25	Skull fractured 1 month before onset of typhoid fever; during typhoid, signs of meningitis and intracranial abscess at site of fracture	Operation: suppurative meningitis with abscess at site of fracture of skull	B. typhosus from localized cerebrospinal meningitis	B. typhosus from blood culture.
8	1908	Henry and Rosenberger	M	34	Seen on 6th day of disease after onset of meningitis; death 3 days later	Purulent meningitis; early lesions of typhoid in intestine	B. typhosus from spinal fluid by lumbar puncture	Blood contained B. typhosus.

9	1908	Southard and Richards	M 32	Patient was a pariete who had been in the asylum for 1 year; he died in coma after an acute illness of 1 week	Lesions of taboparosis; acute cerebrospinal meningitis, with polymorphonuclear exudate; no intestinal lesions of typhoid	B. typhosus from spinal fluid, brain and mesenteric lymph node	Aside from mesenteric lymphadenitis, no lesions of typhoid infection outside of the nervous system.
10	1909	Symmers and Wilson	M 37	Illness of 10 days with symptoms of serous meningitis; death on 15th day	None	B. typhosus from purulent spinal fluid after death	Widal reaction positive on 13th day.
11	1912	Milligan	M 47	Meningitic syndrome on 3d day of typhoid fever; death on 5th day	Purulent cerebrospinal meningitis; typhoid ulcers in ileum	B. typhosus from meninginges	Blood culture gave B. typhosus; white blood cells, 10,000.
12	1912	Lesieur and Marchand	M 41	Meningitis on 28th day of typhoid; death next day	Purulent meningitis; no intestinal lesions	B. typhosus from spinal fluid	B. typhosus from blood culture.
13	1912	O'Carroll and Purser	M 9	Convulsions on 5th day of typhoid fever and death 1 day later	Yellow pus in meninginges; congestion and swelling of Peyser's patches	B. typhosus from spinal fluid before and after death	Widal positive.
14	1914	Planché and Lombard	M 2	Meningitis after 24 days of enteritis and pneumonia; death 3 days later	"Intestines absolutely normal;" purulent meningitis; pneumonia	B. typhosus from purulent spinal fluid	Pneumococcus from lung; leukocytes showed 85 per cent. mononuclears.
15	1914	Planché and Lombard	M 8	Meningitis on 35th day of typhoid; death in coma next day	Typhoid lesions in intestines; suppurative meningitis	B. typhosus from spinal fluid	
16	1915	Robinson	M 55	Outspoken meningitis on 2d day; death on 4th	None	B. typhosus on repeated cultures of purulent spinal fluid	Reported as "primary typhoid meningitis."
17	1915	Ortoconi and Amelle	M 28	Soldier in French Army; stuporous until 3d day, when onset of meningitis; death next day	Purulent meningitis; ulcers in ileum	B. typhosus from spinal fluid	Borderline case between serous and purulent meningitis.
18	1915	Author's case					

As an addition to Table II might be added a case reported by Arzt and Boese, in 1908, in which it was demonstrated that *B. paratyphosus* was the cause of purulent meningitis in a child seven weeks old.

PURULENT MENINGITIS. A review of the literature shows that purulent meningitis due to the typhoid bacillus is both an uncommon form of meningeal disease and also a rare phase of typhoid infection. Bramwell states that the meningococcus causes 50 per cent. and the pneumococcus 42 per cent. of cases of acute primary meningitis. In addition, leptomeningitis may be caused by many organisms, as a secondary process to a focus of infection elsewhere in the body. Though no definite statistics are available, it is readily seen that after the elimination of cases of meningitis due to the tubercle bacillus, the pneumococcus, and the pyogenic cocci there remain only a few to be accounted for by the organisms of influenza, diphtheria, gonorrhea, and typhoid fever. Out of 2768 cases of typhoid fever seen in this hospital between the years 1890 and 1916, there have been 5 cases of purulent meningitis due to *B. typhosus*. During the same period, among the adult patients of the medical clinic, there have been 290 cases of all forms of meningitis, of which 5 were caused by the typhoid bacillus. These figures give an incidence of 0.2 per cent. for meningitis in typhoid fever and 1.75 per cent. for typhoid meningitis among the bacterial meningeal diseases. Since 1904, when Cole published a collection of 15 cases, reports of 17 additional instances of purulent typhoid meningitis have appeared. These together with the case described in this paper are summarized in Table II. In all cases included in this compilation, except Nos. 2 and 3, the identification of the typhoid bacillus in the spinal fluid has been placed beyond question by detailed cultural and serological studies.

The data furnished by these cases indicate that purulent meningitis may occur at any time during the course of typhoid infection. Aside from the cases regarded as "primary typhoid meningitis," instances are presented of the occurrence of meningitis on any day of the disease from the second to the thirty-fifth. A striking fact is the invariably fatal outcome of all cases of generalized typhoid meningitis, and that usually within three days of the onset of the meningeal symptoms. The spinal fluid in a typical case is turbid, with a yellowish tinge. Typhoid bacilli are usually demonstrable in smear preparations of the fluid, and must be found by cultures before the diagnosis can be established. While the cells of the fluid are accumulations of polymorphonuclear leukocytes, the white corpuscles of the blood are usually not much increased; rarely above 10,000. In the case reported in this paper they did not rise above 5200 per cmm. The differential count of the leukocytes has varied greatly. Planché and Lombard report 85 per cent. mononuclears in the blood of their case, while in our case there were 85 per cent. polymorphonuclear neutrophils. The presence or absence of bronchopneumonia may have so great an influence on the blood picture that no definite conclusions can be drawn from these figures.

REPORT OF CASE. *Diagnosis: Typhoid fever (B. typhosus); purulent cerebrospinal meningitis; bronchopneumonia.*

The patient, I. J., a negress, aged nineteen years, was admitted to the medical service of the Johns Hopkins Hospital (Gen. No. 103845) on July 19, 1915. The patient was partially comatose when brought to the hospital. Her mother said that her daughter had been ill with typhoid fever for three weeks. Until the onset of this sickness the patient had never had any severe illness. For several days in the last week of June, 1915, she had had headache and dizziness. It was known on July 1 that she had fever, but she was not confined to bed until July 12, when she became prostrated and irrational. After that date a restless stupor supervened and the patient began to complain of headache and soreness in the neck.

On July 19 *physical examination* showed her to be a large, obese young negress, semicomatose, slightly jaundiced, and polypneic. Her temperature was 104° F.; pulse 132 per minute; respirations 40 per minute. The neck, slightly retracted, was painful when flexed, and Kernig's sign was slightly positive. The physical signs in the chest were those of bronchopneumonia of the lower lobes of both lungs. The abdomen was slightly distended and painful when palpated; the spleen could not be felt. The white blood cells were 5520 per mm., with 83 per cent. polymorphonuclear leukocytes.

The signs of meningeal disease were so striking that a lumbar puncture was done at once. The spinal fluid appeared under normal pressure, was clear, watery, contained 6 cells per mm., and gave a faintly positive globulin reaction by the Ross-Jones test. In the blood and spinal fluid the Wassermann reaction was negative, and the gold chloride reaction with the spinal fluid was normal. Cultures from the spinal fluid were negative.

On July 20 *B. typhosus* was grown from the blood culture and the Widal reaction was positive for the typhoid bacillus in dilution of 1 to 100. Throughout this day the patient's condition remained essentially unchanged. In the evening she became very stuporous, and a slight strabismus of the right eye appeared.

On July 21 she brightened mentally, but there was a definite divergent strabismus, slight rigidity of the neck, and absent patellar reflexes. She had been receiving ice-water sponges, and during this day her temperature did not rise above 102° F.

On July 22 her temperature rose rapidly to 103° F. She groaned continually in a restless stupor. At 10.30 p.m., with a temperature of 104° F., the white blood cells were 5200. At midnight, when her temperature was 106° F., she suddenly passed into clonic convulsions and became unconscious. There were violent jerking movements of all parts of the face, trunk, arms, and legs, and when the eyes were relatively still they showed a widely divergent strabismus. At this time her neck became readily flexible, the knee-jerks were elicited for the first time, and Kernig's sign was

no more positive than on her admission. After convulsions lasting for two hours the patient died. Lumbar puncture done during these agonal convulsions gave a turbid greenish-yellow spinal fluid under pressure of more than 200 mm. of water. The cells, not counted, formed a pavement of pus when spread on a microscopic slide. In stains for bacteria no organisms of any sort were discoverable. Cultures of the spinal fluid, however, yielded *B. typhosus* alone. This organism gave the typical cultural reactions of the typhoid bacillus and was agglutinated by a dilution of 1 to 3200 of the serum of a rabbit immunized with the laboratory's strain of *B. typhosus*. In making the cultures, varying amounts of the spinal fluid, were placed in several tubes of bile-broth and agar. Growth of the bacillus, however, occurred only in one tube. This, together, with the fact that no bacteria could be found in stained smears of the fluid, clearly indicates that very few bacilli were present, and suggests the manner in which the cause of an obscure case of meningitis might be overlooked.

Postmortem Examination. (No. 4410. Dr. R. Major. July 23, 1915.)

Summary of the Protocol. The subject was a large-framed, well-nourished negress, with slightly jaundiced conjunctivæ. Both pleural cavities were obliterated by dense fibrous adhesions. The lungs were extensively consolidated with areas of *bronchopneumonia*.

Intestine. The mucosa of the ileum near the ileocecal valve showed several round, raised, buttonhole-like ulcers, with necrotic material on their surfaces. The lymph follicles of the ileum and cecum were enlarged, and the mesenteric lymph nodes were large and soft.

Spleen. The spleen weighed 230 grams and showed the characteristic "acute splenic tumor" of infection. The liver weighed 1870 grams. The section of this organ showed extensive fatty change and areas of central necrosis. In the other organs, except the central nervous system, there were no significant abnormalities.

Brain. The meninges on the surface of the brain disclosed a considerable accumulation of yellowish-white creamy exudate. The greatest amount of this exudate was at the base of the brain, but along with the engorged bloodvessels, it continued upward over the convexity, fading out at the upper margins of the temporal lobes. The microscopic picture of this meningeal lesion corresponded with that described by MacCallum. In the arachnoid spaces and around the bloodvessels there were dense accumulations of polymorphonuclear cells. Near the pial vessels, penetrating the cortex, were a few large mononuclear cells, with inclusions in their cytoplasm, evidently the endothelial phagocytes described by MacCallum. The exudative process, however, did not affect the cortical substance of the brain. No bacteria were seen in this exudate.

SUMMARY. This report describes a case of purulent cerebrospinal meningitis due to *B. typhosus*, occurring in the fourth week of a typical case of typhoid fever. The outcome, as in similar cases, was lethal within a few days after the onset of the meningitis.

Statistics of the medical clinic of the Johns Hopkins Hospital show that out of 2768 cases of typhoid fever there have been 5 cases of typhoid meningitis. Seventeen case reports of this relatively rare phase of typhoid infection are summarized from the literature on the subject. These, together with the 15 cases collected by Cole, and with the case reported herein make a total of 33 proved accounts of the condition in the statistics of typhoid fever.

From these articles are collected comparative data on the spinal fluid in meningism, serous meningitis, and purulent meningitis.

Several cases of so-called "primary typhoid meningitis" are emphasized here, since lacking intestinal lesions, the mode of infection is obscure.

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